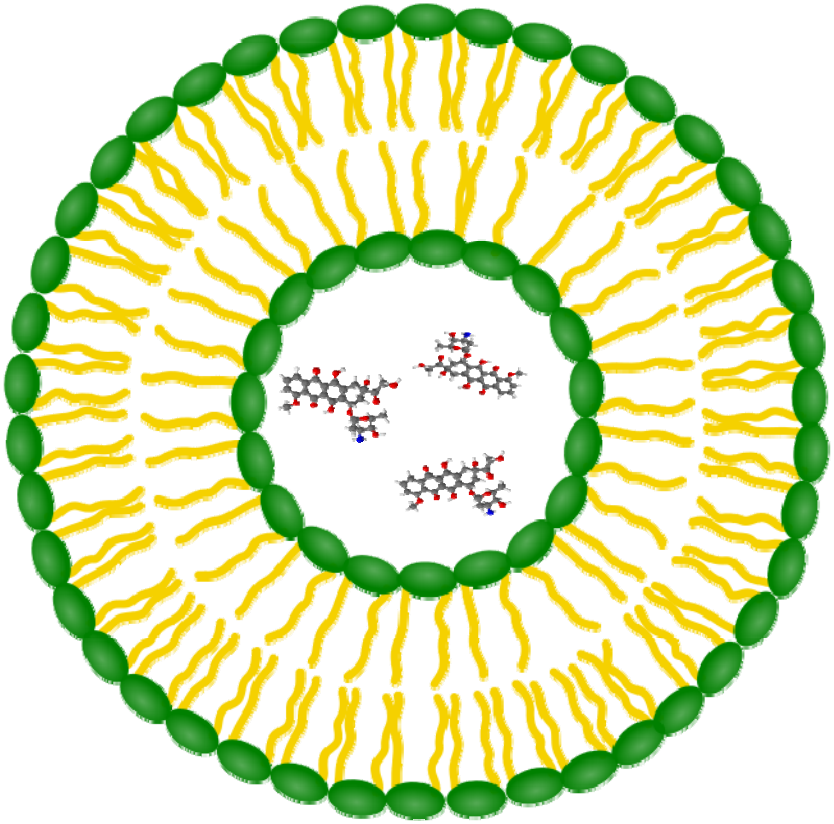
Drug Delivery with Temperature Sensitive Liposomes



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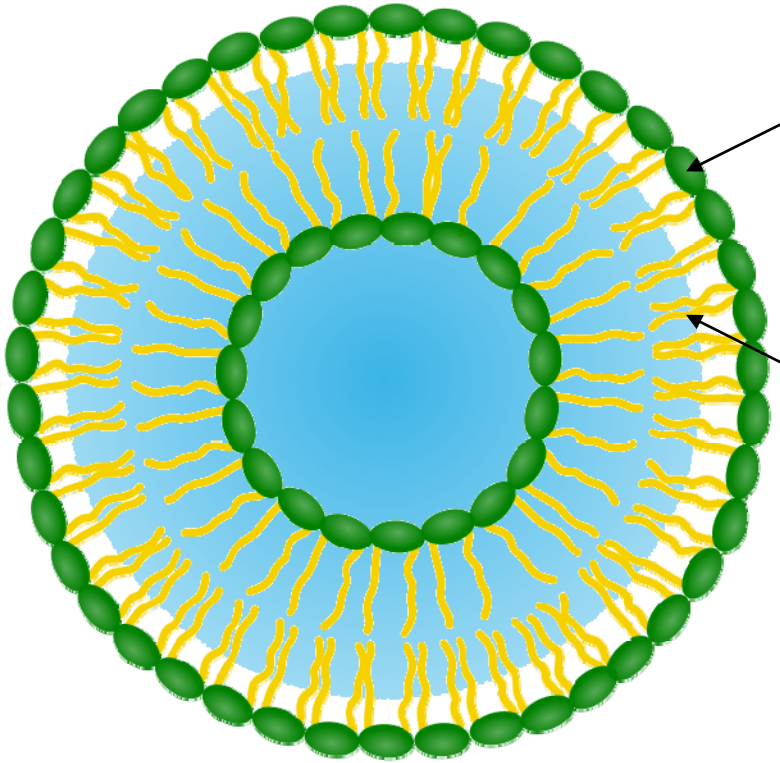
- Department of Chemical Engineering
- Mentor: Tallie Forbes

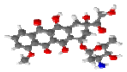
- Funding from National Institutes of Health (NIH)

Liposomes and Mechanism

- Phospholipid bilayer (cell membrane material)



Mechanism:



Drug permeates membrane and is encapsulated

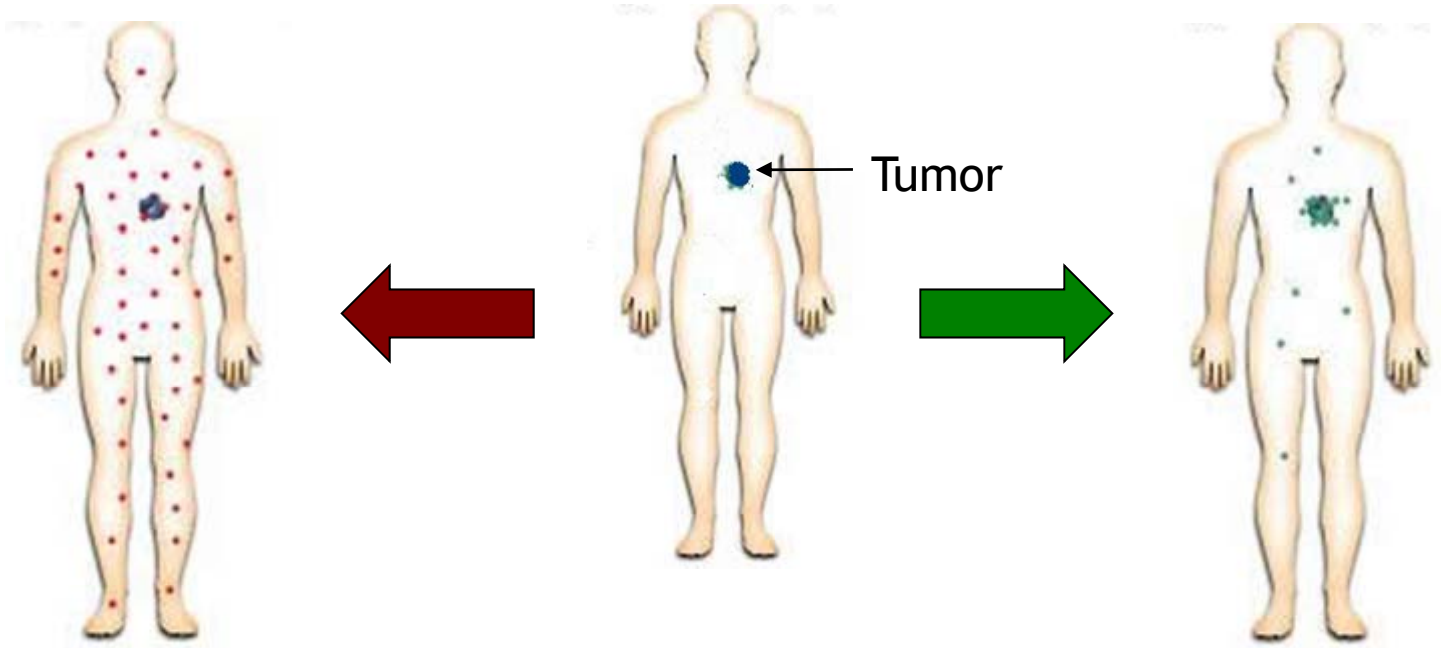
Distinguishing Characteristic

- Naturally aggregates in “leaky” cancer tissue
- Temperature Sensitive

(releases contents at ~40° C)

Big Picture

➔ More effective cancer treatments by using temperature sensitive liposomes as vehicles for chemotherapy drugs



Current Chemotherapy

- Dispersed
- Limited dosages
- Wide range of adverse effects

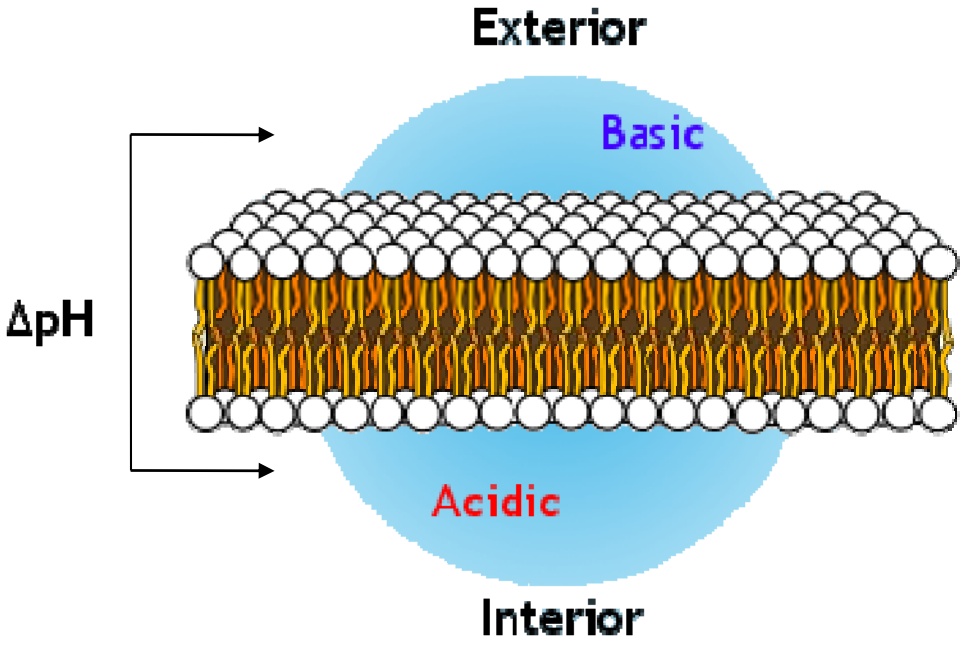
Liposome Delivery

- Targeted
- Larger effective dosage
- Reduced adverse effects
- Controlled release

Research Goals

➔ What loading conditions give the highest encapsulation efficiency?

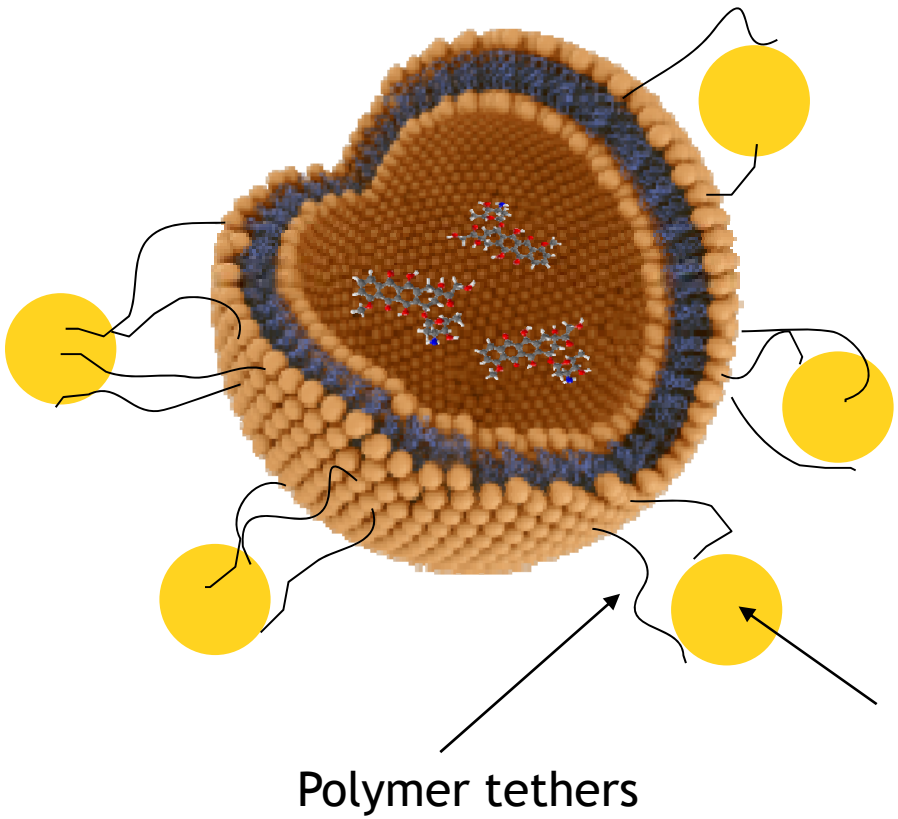
$$\frac{\text{amount of drug encapsulated}}{\text{total drug added to sample}} = \text{encapsulation efficiency}$$



Variables

- pH gradient (ΔpH)
- Temperature
- Time
- Concentrations

- Using gold nanoshells for controlled release



Mechanism

1) Tethering of nanoshells to liposome
2) Irradiation with near-infrared laser
3) Liposome is heated to release temperature
4) Drug is released

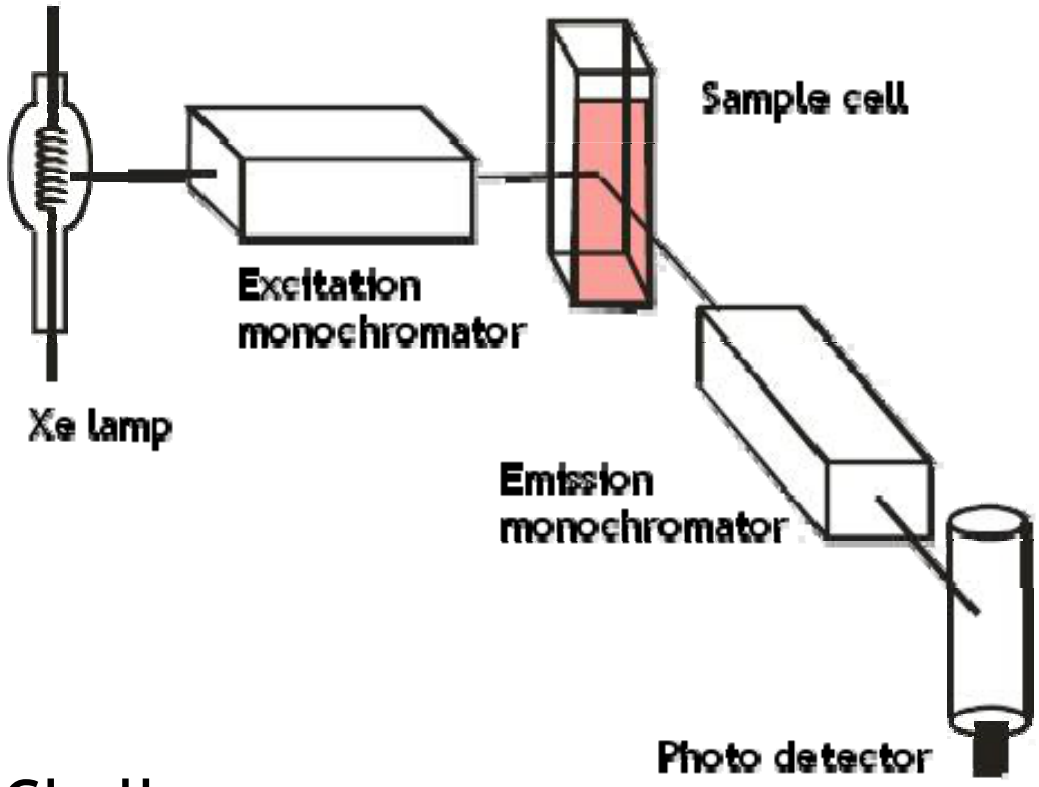
Method: Fluorescence Spectroscopy

- Measuring concentration of drug through fluorescence intensity

Generally, intensity is directly related to concentration:

$$I = kC$$

Proportionality constant



- Fluorescence is measured before and after rupturing loaded liposomes

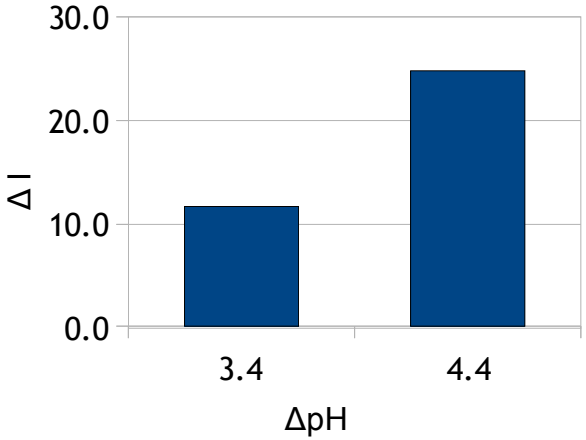
Challenges

- Photodecomposition
- Self-quenching
- Chemical interaction

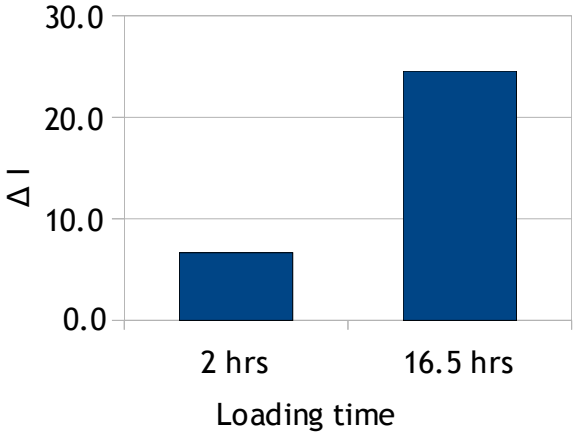
Preliminary Results: Encapsulation

- Change in fluorescence intensity (ΔI) is indicative of how much drug was encapsulated

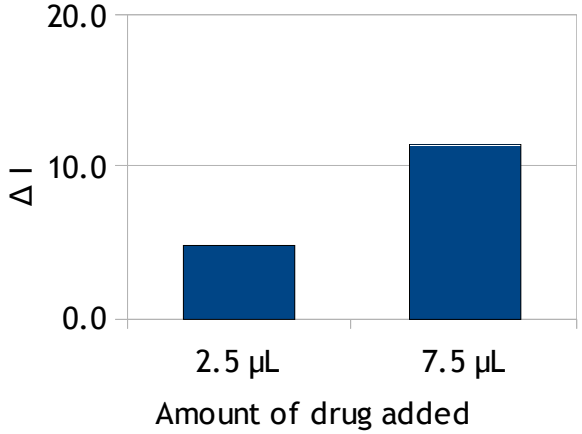
Increased pH Gradient



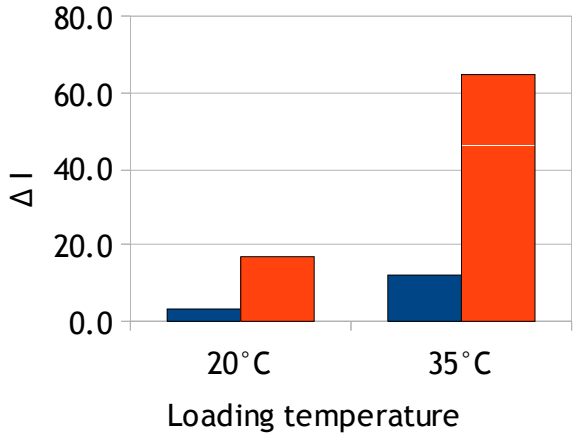
Increased Loading Time

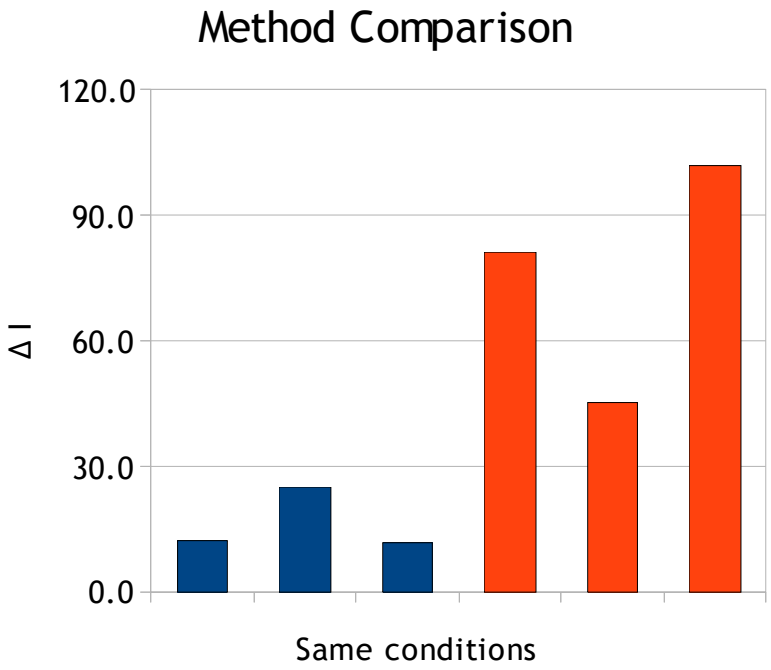


Increased Drug Amount



Increased Loading Temperature





Two loading schemes used

- Double buffer method
  - Manually established pH gradient
- Ion gradient method
  - Passively established pH gradient

Summary

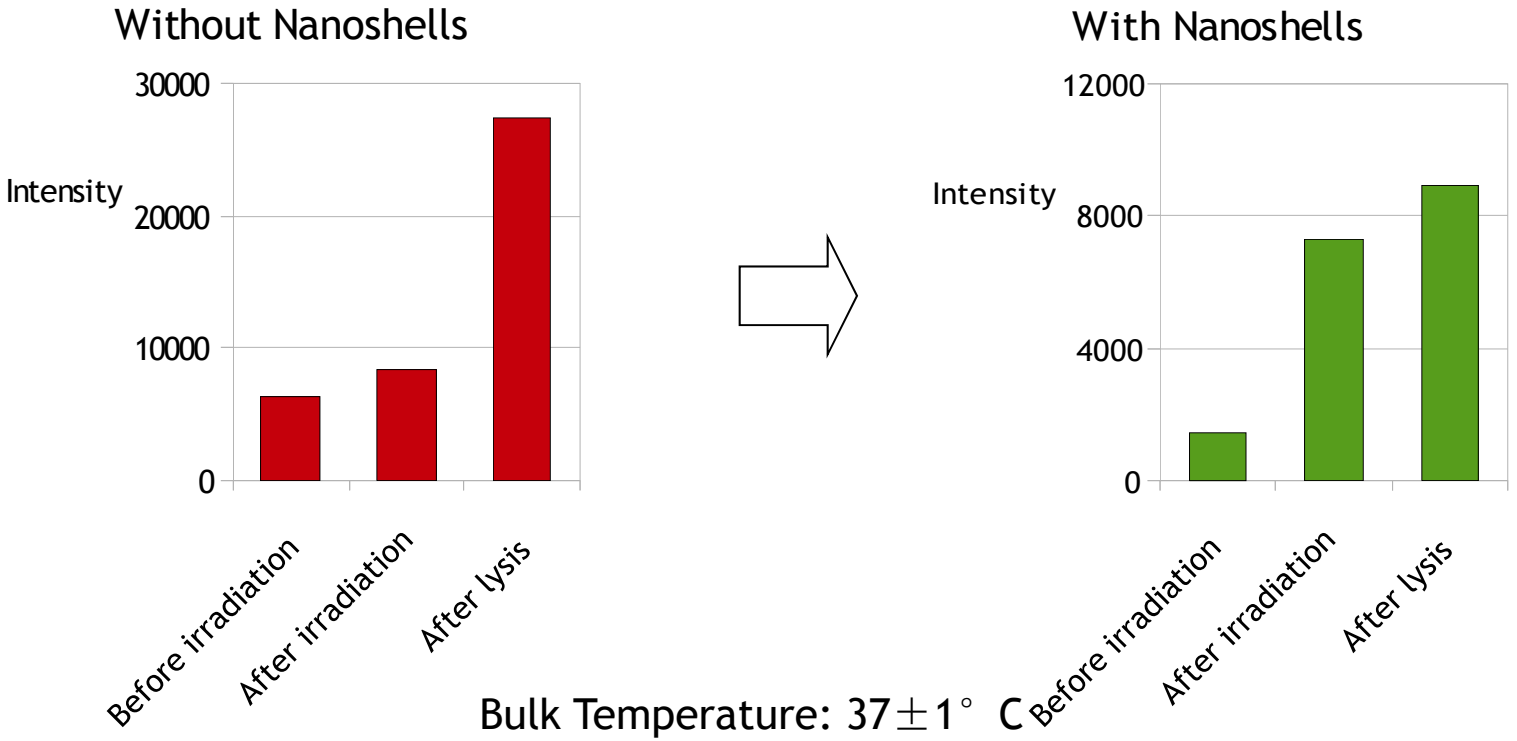
Increases in encapsulation seen when:

- pH gradient is increased
- Loading time is increased
- Loading temperature is increased
- Drug to lipid ratio is increased

- Ion gradient loading shows to be much more efficient

Preliminary Results: Release

- Loaded liposomes irradiated with near-infrared laser

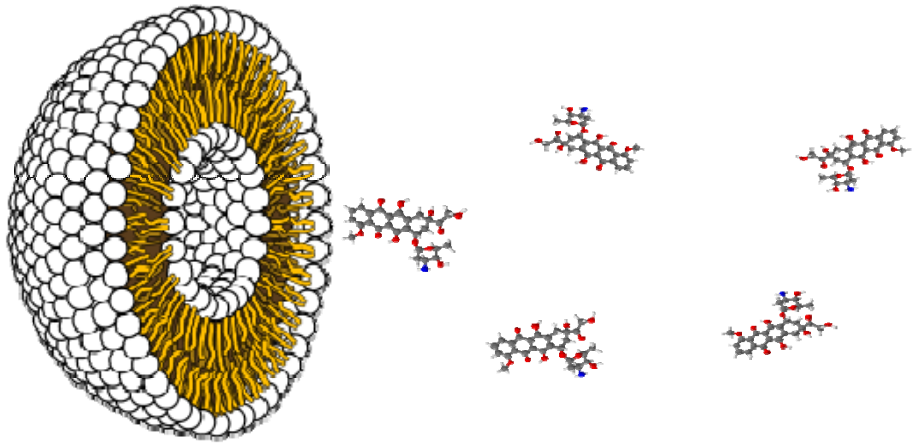


Bulk Temperature: 37±1° C
Release Temperature: 40° C

78.71% Release

Conclusions

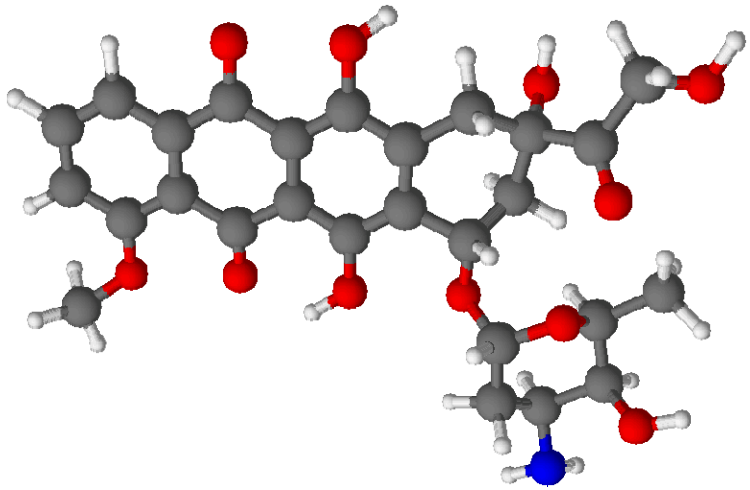
- Increasing encapsulation trend with increasing loading time, temperature, pH gradient and drug/lipid ratio
- Ion gradient loading much more effective



- Significant release observed with nanoshells, suggests relatively effective nanoshell tethering

Future Work:

- Leakage measurement
- Comparative release with different tethering methods
- More encapsulation data, specifically regarding time and concentration



Acknowledgments

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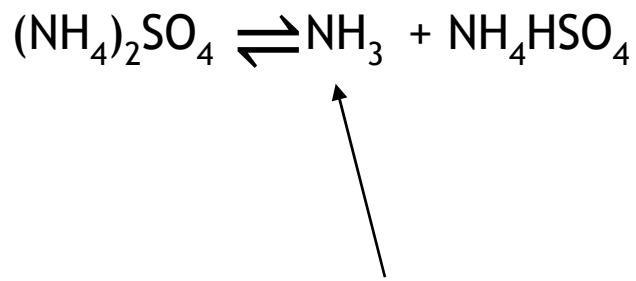
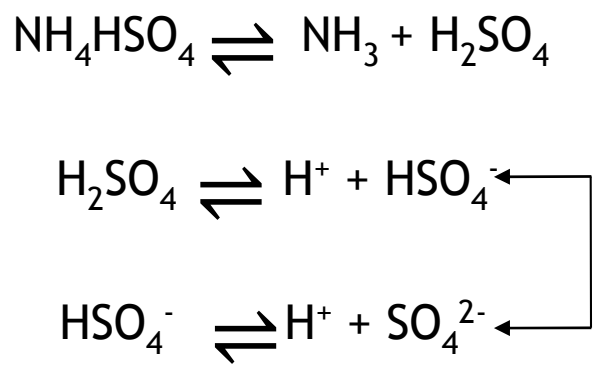
Ion Gradient Method



Uncharged (leaves the liposome)

Further equilibria:



Acidification of interior